

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-9. (Cancelled)

10. (new) A method for the treatment:

- of pathologies requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or
- of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation,  
said method comprising the administration of a pharmaceutically acceptable amount:
  - of a protein characterized in that it comprises or is constituted by:
    - \* the NOV protein, represented by the sequence SEQ ID NO: 2, or
    - \* a fragment of this protein, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in

particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

- \* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or
- \* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity,

– or of a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:

- \* either for the NOV protein as defined above,
- \* or for a fragment of the NOV protein as defined above,
- \* or for a sequence derived from the NOV protein as defined above,
- \* or for a sequence homologous to the NOV protein as defined above,

said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the

sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12,  
– or of an anti-idiotypic antibody of the NOV protein.

11. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

- \* the NOV protein, represented by the sequence SEQ ID NO: 2, or
- \* a fragment of this protein, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or
- \* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or
- \* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence

SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

12. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by the NOV protein, represented by the sequence SEQ ID NO: 2.

13. (new) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

\* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,

SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

\* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

\* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

**14. (new)** A method for the treatment of cancer, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

\* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,

SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

\* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

\* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

15. (new) A pharmaceutical composition characterized in that it contains as active ingredient:

- a protein characterized in that it comprises or is constituted by:
  - \* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or
  - \* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or
  - \* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined below, preferably having a homology of at least

approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity, or

– a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:

- \* either for the NOV protein as defined above,
- \* or for a fragment of the NOV protein as defined above,
- \* or for a sequence derived from the NOV protein as defined above,
- \* or for a sequence homologous to the NOV protein as defined above,

said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12, or

- an anti-idiotypic antibody of the NOV protein,

in combination with a pharmaceutically acceptable vector.

**16. (new)** The pharmaceutical composition according to claim 15, characterized in that it contains as active ingredient a protein characterized in that it comprises or is constituted by:

\* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6,  
SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

\* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

\* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity,

in combination with a pharmaceutically acceptable vector.

17. (new) The pharmaceutical composition according to claim 15, characterized in that it contains as active ingredient the sequence SEQ ID NO: 8.

18. (new) A method for the treatment:

– of pathologies requiring the inhibition of endothelial proliferation, in particular within the framework of the following pathologies: age-related macular degeneration, diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma, or

– of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation,

said method comprising the administration of a pharmaceutical composition characterized in that it contains as active ingredient:

– a protein characterized in that it comprises or is constituted by:

\* a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

\* any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or

\* any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined below, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity, or

– a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding:

- \* either for the NOV protein as defined above,
- \* or for a fragment of the NOV protein as defined above,
- \* or for a sequence derived from the NOV protein as defined above,
- \* or for a sequence homologous to the NOV protein as defined above, said nucleotide sequence corresponding in particular to the nucleotide sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO: 12, or
- an anti-idiotypic antibody of the NOV protein,

in combination with a pharmaceutically acceptable vector,  
said pharmaceutical composition being administered at a rate of approximately 0.1  
to approximately 20 mg/kg/day.